RCT
Potential PURL Review Form
PURL Jam Version

PURLs Surveillance System
Family Physicians Inquiries Network

SECTION 1: Identifying Information for Nominated Potential PURL
[to be completed by PURLs Project Manager]

A. Citiation: Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, Navaneethan SD, Singh RP, Pothier CE, Nissen SE, Kashyap SR; STAMPEDE Investigators. Bariatric Surgery versus Intensive Medical Therapy for Diabetes - 5-Year Outcomes. N Engl J Med. 2017 Feb 16;376(7):641-651. doi: 10.1056/NEJMoa1600869. PubMed PMID: 28199805; PubMed Central PMCID: PMC5451258.
B. Link to PubMed Abstract: https://www.ncbi.nlm.nih.gov/pubmed/?term=28199805
C. First date published study available to readers: 2/16/2017
D. PubMed ID: 28199805
E. Nominated By: Jennie Jarrett
F. Institutional Affiliation of Nominator: University of Illinois at Chicago
G. Date Nominated: 2/16/2017
H. Identified Through: NEJM
I. PURLs Editor Reviewing Nominated Potential PURL: Corey Lyon
J. Nomination Decision Date: 3/8/2018
K. Potential PURL Review Form (PPRF) Type: RCT
L. Assigned Potential PURL Reviewer: Kortnee Y Roberson
M. Reviewer Affiliation: University of Chicago
A. Abstract: BACKGROUND:
Long-term results from randomized, controlled trials that compare medical therapy with surgical therapy in patients with type 2 diabetes are limited.

METHODS:
We assessed outcomes 5 years after 150 patients who had type 2 diabetes and a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 27 to 43 were randomly assigned to receive intensive medical therapy alone or intensive medical therapy plus Roux-en-Y gastric bypass or sleeve gastrectomy. The primary outcome was a glycated hemoglobin level of 6.0% or less with or without the use of diabetes medications.

RESULTS:
Of the 150 patients who underwent randomization, 1 patient died during the 5-year follow-up period; 134 of the remaining 149 patients (90%) completed 5 years of follow-up. At baseline, the mean (±SD) age of the 134 patients was 49±8 years, 66% were women, the mean glycated hemoglobin level was 9.2±1.5%, and the mean BMI was 37±3.5. At 5 years, the criterion for the primary end point was met by 2 of 38 patients (5%) who received medical therapy alone, as compared with 14 of 49 patients (29%) who underwent gastric bypass (unadjusted P=0.01, adjusted P=0.03, P=0.08 in the intention-to-treat analysis) and 11 of 47 patients (23%) who underwent sleeve gastrectomy (unadjusted P=0.03, adjusted P=0.07, P=0.17 in the intention-to-treat analysis). Patients who underwent surgical procedures had a greater mean percentage reduction from baseline in glycated hemoglobin level than did patients who received medical

therapy alone (2.1% vs. 0.3%, P=0.003). At 5 years, changes from baseline observed in the gastric-bypass and sleeve-gastrectomy groups were superior to the changes seen in the medical-therapy group with respect to body weight (-23%, -19%, and -5% in the gastric-bypass, sleeve-gastrectomy, and medical-therapy groups, respectively), triglyceride level (-40%, -29%, and -8%), high-density lipoprotein cholesterol level (32%, 30%, and 7%), use of insulin (-35%, -34%, and -13%), and quality-of-life measures (general health score increases of 17, 16, and 0.3; scores on the RAND 36-Item Health Survey ranged from 0 to 100, with higher scores indicating better health) (P<0.05 for all comparisons). No major late surgical complications were reported except for one reoperation.

CONCLUSIONS:
Five-year outcome data showed that, among patients with type 2 diabetes and a BMI of 27 to 43, bariatric surgery plus intensive medical therapy was more effective than intensive medical therapy alone in decreasing, or in some cases resolving, hyperglycemia. (Funded by Ethicon Endo-Surgery and others; STAMPEDE ClinicalTrials.gov number, NCT00432809 .).

B. Pending PURL Review Date**:** 2/8/2018

SECTION 2: Critical Appraisal of Validity
[to be completed by the Potential PURL Reviewer]

A. Number of patients starting each arm of the study?
Original study: 218 participants, 150 included. 50 in each arm (intensive medical therapy, gastric bypass, sleeve gastrectomy)
Five year follow up: 149 included. One patient died during 5-year follow up period. 134 participants completed five year follow-up. 38 intensive medical therapy, 49 gastric bypass, 47 sleeve gastrectomy

B. Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)
Inclusion: age 20 to 60 years, hgba1c level more than 7.0% and BMI of 27 to 43.
Exclusion: undergone previous bariatric surgery or other complex abdominal surgery or poorly controlled medical or psych disorders.
Single center study, 66% women, mean age 49+/-8 years,

C. Intervention(s) being investigated?
Intensive medical therapy
Intensive medical therapy + gastric bypass
Intensive medical therapy + sleeve gastrectomy

D. Comparison treatment(s), placebo, or nothing?
Intensive medical therapy, gastric bypass, gastrectomy

E. Length of follow-up? (Note specified end points, e.g., death, cure, etc.)
5 year follow up – primary end pinpoint: hgba1c 6.0 or less

F. What outcome measures are used? List all that assess effectiveness.
Primary outcome: hgba1c of 6.0 or less
Secondary outcome: hgba1c # of pts and %, median fasting plasma glucose, body weight, lipid levels, renal function, ophthalmologic outcomes, medication use, systolic and diastolic blood pressure, adverse events, and quality of life (RAND 36-items Health Survey)

G. What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CU, p-values, etc.
Hgba1c less than or equal to 6.0%
- intensive medical therapy group 2 of 38 (5.3%)
- gastric bypass group 14 of 49 (29%) P=0.01 unadjusted, adjusted P0.03, P 0.08 intention to treat analysis.
- sleeve-gastrectomy group 11 of 47 (23%) P=0.03 unadjusted, adjusted P 0.07, P=0.17 intention to treat analysis

H. What are the adverse effects of intervention compared with no intervention?
Intensive medical therapy group: MI, excessive weight gain
Gastric bypass: gastrointestinal bleeding, severe hypoglycemia requiring intervention, ketoacidosis
Sleeve gastrectomy: stroke, gastrointestinal leak, sepis

I. The study addresses an appropriate and clearly focused question.
(select one) Well covered

Comments:

J. Random allocation to comparison groups:
(select one) Well covered

Comments:

K. Concealed allocation to comparison groups:
(select one) Well covered

Comments:

L. Subjects and investigators kept “blind” to comparison group allocation:
(select one) Adequately addressed

Comments:

M. Comparison groups are similar at the start of the trial:
(select one) Well covered
Comments:

N. Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential sources of bias. (select one) Well covered
Comments:

O. Were all relevant outcomes measured in a standardized, valid, and reliable way?
(select one) Adequately addressed
Comments:

P. Are patient oriented outcomes included? If yes, what are they?
Yes, decreased hgba1c. weight loss, quality of life, blood pressure, lipid levels, renal function, mediation use

Q. What percent dropped out, and were lost to follow up? Could this bias the results? How?

9 pts didn't start assigned treatment and withdrew immediately after randomization or during initial 6 months after randomization. 8 in medical therapy, 1 in sleeve-gastrectomy group. 6 patients lost to follow up. 1 pt died of MI during year 4. 1 pt in medical therapy underwent gastric bypass due to failure of medical therapy in year 3. Year 4 one patient in sleeve group underwent gastric bypass for treatment of gastric fistula.

R. Was there an intention-to-treat analysis? If not, could this bias the results? How?
yes

S. If a multi-site study, are results comparable for all sites?
Single study site

T. Is the funding for the trial a potential source of bias? If yes, what measures were taken to ensure scientific integrity? Yes, the sponsors were not involved in analysis of data or article.

U. To which patients might the finding apply? Include patients in the study and other patients to whom the findings may be generalized.
Patients with diabetes or chronic conditions related to obesity

V. In what care settings might the finding apply, or not apply?
Outpatient.

W. To which clinicians or policy makers might the finding be relevant?
Primary care physicians, endocrinologist

SECTION 3: Review of Secondary Literature
[to be completed by the Potential PURL Reviewer]
[to be revised by the Pending PURL Reviewer as needed]

Citation Instructions:

For up-to-date citations, use style modified from http://www.uptodate.com/home/help/faq/using_UTD/index.html#cite & AMA style. Always use Basow DS on editor & current year as publication year.

Example: Auth I. Title of article. {insert author name if given, & search terms or title.} In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2009. Available at: http://www.uptodate.com. {Insert date modified if given.} Accesses February 12, 2009. [whatever date PPRF reviewer did their search.}

For DynaMed, use the following style:
Depression: treatment {insert search terms or title}. In: DynaMed [database online]. Available at http://www.DynamicMedical.com. Last updated February 4, 2009. {Insert date modified if given.} Accessed June 5, 2009. {search date}

DynaMed excerpts Bariatric surgery is recommended to improve glycemic control in appropriate surgical candidates with (Strong recommendation):

- body mass index (BMI) ≥ 40 kg/m^2 (≥ 37.5 kg/m^2 in Asian Americans) regardless of complexity of glucose-lowering regimens and level of glycemic control
- BMI of 35-39.9 kg/m^2 (32.5-37.4 kg/m^2 in Asian Americans) and hyperglycemia is inadequately controlled despite lifestyle changes and optimal medical therapy

Roux-en-Y gastric bypass may cause greater weight loss compared to laparoscopic adjustable gastric banding or intensive lifestyle weight loss intervention in patients with type 2 diabetes (level 2 [mid-level] evidence)
bariatric surgery appears to increase diabetes remission and reduce diabetes medication compared to intensive lifestyle weight loss intervention in patients with obesity and type 2 diabetes (level 2 [mid-level] evidence)
bariatric surgery associated with increased diabetes remission at 15 years compared to nonsurgical treatment (level 2 [mid-level] evidence)
addition of bariatric surgery to intensive medical therapy associated with improved glycemic control up to 5 years in patients with mild-to-moderate obesity and uncontrolled type 2 diabetes (level 3 [lacking direct] evidence)
bariatric surgery reported to reduce diabetes medication use and long-term healthcare costs in adults with type 2 diabetes (level 3 [lacking direct] evidence)
bariatric surgery appears more effective than nonsurgical management for long-term weight loss and recovery from diabetes and hypertension (level 2 [mid-level] evidence)

A. DynaMed citation/Management of type 2 diabetes in adults. In: DynaMed [database online]. Available at:
access date www.DynamicMedical.com Last Updated: . January 11, 2018 Accessed February 7, 2018

B. Bottom line recommendation orsummary of evidence from DynaMed (1-2 sentences)
American Diabetes Association (ADA) uses the term metabolic surgery rather than bariatric surgery to reinforce the role of surgery in treatment of type 2 diabetes[1]

- metabolic surgery for patients with type 2 diabetes mellitus
  - recommend when (ADA Grade A)
    - body mass index (BMI) is ≥ 40 kg/m^2 (≥ 37.5 kg/m^2 in Asian Americans) regardless of complexity of glucose-lowering regimens and level of glycemic control
    - BMI is 35-39.9 kg/m^2 (32.5-37.4 kg/m^2 in Asian Americans) and hyperglycemia is inadequately controlled despite lifestyle changes and optimal medical therapy
  - consider when BMI is 30-34.9 kg/m^2 (27.5-32.4 kg/m^2 in Asian Americans) and hyperglycemia is inadequately controlled despite optimal medical control by either oral or injectable medication (including insulin) (ADA Grade B)

UpToDate excerpts **SURGICAL TREATMENT OF OBESITY** — Surgical treatment of obesity is an option to treat type 2 diabetes in appropriate surgical candidates with [55,56]:

●BMI (body mass index) ≥40 kg/m^2 (BMI ≥37.5 kg/m^2 in Asian Americans)

●BMI 35 to 39.9 kg/m^2 (BMI 32.5 to 37.4 kg/m^2 in Asian Americans) when hyperglycemia is inadequately controlled by lifestyle measures and optimal medical therapy

For selected obese patients with type 2 diabetes (appropriate surgical candidates with BMI ≥40 kg/m^2 or BMI 35 to 39.9 kg/m^2 when hyperglycemia is inadequately controlled by lifestyle measures and optimal medical therapy), we suggest bariatric surgery (**Grade 2B**). However, longer-term follow-up of clinically important endpoints, such as effects on microvascular and macrovascular

complications and mortality, are required before bariatric surgery procedures can be routinely recommended for the treatment of persistent hyperglycemia, resistant to multiple medications, in obesity-related type 2 diabetes. (See 'Surgical treatment of obesity' above.)

C. UpToDate citation/ Always use Basow DS as editor & current year as publication year. Access date Title. Author.David K McCulloch In: UpToDate [database online]. Management of persistent hyperglycemia in type 2 diabetes mellitus. Available at: http://www.uptodate.com. Last updated April 13, 2017: . Accessed February 7, 2018

D. Bottom line recommendation or summary of evidence from UpToDate (1-2 sentences)
Surgical treatment of obese patients with diabetes results in the largest degree of sustained weight loss (20 to 30 percent after one to two years) and, in parallel, the largest improvements in blood glucose control. However, there are no long-term, high-quality studies (randomized trials) on improvement in microvascular and macrovascular complications.

E. Other excerpts (USPSTF; other guidelines; etc.)

F. Citations for other excerpts

G. Bottom line recommendation or summary of evidence from Other Sources (1-2 sentences)

SECTION 4: Conclusions
[to be completed by the Potential PURL Reviewer]
[to be revised by the Pending PURL Reviewer as needed]

A. **Validity**: Are the findings scientifically valid? 2

B. If **A** was coded 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results. Specifically, what is the likely direction in which potential sources of internal bias might affect the results?

C. **Relevance**: Is the topic relevant to the practice of family medicine and primary care practice, including outpatient, inpatient, obstetrics, emergency and long-term care? Are the patients being studied sufficiently similar to patients cared for in family medicine and primary care in the US such that results can be generalized?
1 (extremely well

D. If **C** was coded 4, 5, 6, or 7, please provide an explanation.

E. **Practice changing potential**: If the findings of the study are both valid and relevant, are they not a currently widely accepted recommendation among family physicians and primary care clinicians for whom the recommendation is relevant to their patient care? Or are the findings

likely to be a meaningful variation regarding awareness and acceptance of the recommendation?
1 (definitely a change from current practice)

F. If **E** was coded as 1, 2, 3, or4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

G. **Applicability to a Family Medical Care Setting**:
Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc.), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, education or counseling a patient; or creating a system for implementing an intervention? 1 (definitely could be done in a medical care setting)

H. If **G** was coded as a 4, 5, 6, or 7, please explain.

I. **Immediacy of Implementation**:
Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug, or other essentials available on the market? 3

J. If **I** was coded 4, 5, 6, or 7,please explain why.

K. **Clinically meaningful outcomes or patient oriented outcomes**:
Do the expected benefits outweigh the expected harms? Are the outcomes patient oriented (as opposed to disease oriented)? Are the measured outcomes, if true, clinically meaningful from a patient perspective?
1 (definitely clinically meaningful or patient oriented)

L. If **K** was coded 4, 5, 6, or 7 please explain why.

M. In your opinion, is this a pending PURL? 2

1. Valid: Strong internal scientific validity; the findings appear to be true.

2. Relevant: Relevant to the practice of family medicine.

3. Practice Changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.

4. Applicability in medical setting.

5. Immediacy of implementation

N. Comments on your response for question M.